

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claims 1-9. (Cancelled)

10. (new) A method for the treatment:

- of pathologies requiring the inhibition of endothelial proliferation, in particular within the framework of the following pathologies: age-related macular degeneration, diabetic retinopathy, rheumatoid arthritis, angiomas, angiosarcomas, in particular Castelman's disease and Kaposi's sarcoma, or

- of pathologies requiring the inhibition of endothelial activation, in particular within the framework of the following pathologies: allograft and xenograft rejection, acrocyanosis, scleroderma, or within the framework of the preparation of grafts between collection and transplantation,

said method comprising the administration of a pharmaceutically acceptable amount:

- of a protein characterized in that it comprises or is constituted by:

- * the NOV protein, represented by the sequence SEQ ID NO: 2, or

- * a fragment of this protein, providing that this fragment exhibits an angiogenesis-inhibiting activity, said fragment comprising in particular approximately 40 to approximately 180 amino acids, and being in

particular represented by one of the following sequences SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10 or SEQ ID NO: 12, or

- * any sequence derived from the sequence SEQ ID NO: 2 or from a fragment defined above, in particular by substitution, deletion or addition of one or more amino acids, providing that this derived sequence exhibits an angiogenesis-inhibiting activity, or

- * any sequence homologous to the sequence SEQ ID NO: 2 or to a fragment defined above, preferably having a homology of at least approximately 80%, and in particular 85%, with the region comprised between the amino acids in positions (33) and (338) of the sequence SEQ ID NO: 2, providing that this homologous sequence exhibits an angiogenesis-inhibiting activity,

- or of a nucleotide sequence characterized in that it comprises or is constituted by a nucleotide sequence coding:

- * either for the NOV protein as defined above,
- * or for a fragment of the NOV protein as defined above,
- * or for a sequence derived from the NOV protein as defined above,
- * or for a sequence homologous to the NOV protein as defined above,

said nucleotide sequence corresponding in particular to the nucleotide sequence SEQ ID NO: 1 coding for SEQ ID NO: 2, or to the sequence SEQ ID NO: 3 coding for SEQ ID NO: 4, or to the sequence SEQ ID NO: 5 coding for SEQ ID NO: 6, or to the sequence SEQ ID NO: 7 coding for SEQ ID NO: 8, or to the

sequence SEQ ID NO: 9 coding for SEQ ID NO: 10, or to the sequence SEQ ID NO: 11 coding for SEQ ID NO: 12,

- or of an anti-idiotypic antibody of the NOV protein.

11. (new) The method according to claim 10, comprising the administration of a pharmaceutically acceptable amount of a protein characterized in that it comprises or is constituted by:

- * the NOV protein, represented by the sequence SEQ ID NO: 2, or
- * a fragment of this protein, providing that this fragment exhibits an angiogenesis-inhibiting activity, said fragment comprising in particular approximately 40 to approximately 180 amino acids, and being in particular represented by one of the following sequences SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10 or SEQ ID NO: 12, or
- * any sequence derived from the sequence SEQ ID NO: 2 or from a fragment defined above, in particular by substitution, deletion or addition of one or more amino acids, providing that this derived sequence exhibits an angiogenesis-inhibiting activity, or
- * any sequence homologous to the sequence SEQ ID NO: 2 or to a fragment defined above, preferably having a homology of at least approximately 80%, and in particular 85%, with the region comprised between the amino acids in positions (33) and (338) of the sequence

SEQ ID NO: 2, providing that this homologous sequence exhibits an angiogenesis-inhibiting activity.

12. (new) The method according to claim 10, comprising the administration of a pharmaceutically acceptable amount of a protein characterized in that it comprises or is constituted by the NOV protein, represented by the sequence SEQ ID NO: 2.

13. (new) The method according to claim 10, comprising the administration of a pharmaceutically acceptable amount of a protein characterized in that it comprises or is constituted by:

- * a fragment of the NOV protein, represented by the sequence SEQ ID NO: 2, providing that this fragment exhibits an angiogenesis-inhibiting activity, said fragment comprising in particular approximately 40 to approximately 180 amino acids, and being in particular represented by one of the following sequences SEQ ID NO: 4, SEQ ID NO: 6,

SEQ ID NO: 8, SEQ ID NO: 10 or SEQ ID NO: 12, or

- * any sequence derived from the sequence SEQ ID NO: 2 or from a fragment defined above, in particular by substitution, deletion or addition of one or more amino acids, providing that this derived sequence exhibits an angiogenesis-inhibiting activity, or

* any sequence homologous to the sequence SEQ ID NO: 2 or to a fragment defined above, preferably having a homology of at least approximately 80%, and in particular 85%, with the region comprised between the amino acids in positions (33) and (338) of the sequence SEQ ID NO: 2, providing that this homologous sequence exhibits an angiogenesis-inhibiting activity.

14. (new) A method for the treatment of cancer, comprising the administration of a pharmaceutically acceptable amount of a protein characterized in that it comprises or is constituted by:

* a fragment of the NOV protein, represented by the sequence SEQ ID NO: 2, providing that this fragment exhibits an angiogenesis-inhibiting activity, said fragment comprising in particular approximately 40 to approximately 180 amino acids, and being in particular represented by one of the following sequences SEQ ID NO: 4, SEQ ID NO: 6,

SEQ ID NO: 8, SEQ ID NO: 10 or SEQ ID NO: 12, or

* any sequence derived from the sequence SEQ ID NO: 2 or from a fragment defined above, in particular by substitution, deletion or addition of one or more amino acids, providing that this derived sequence exhibits an angiogenesis-inhibiting activity, or

- * any sequence homologous to the sequence SEQ ID NO: 2 or to a fragment defined above, preferably having a homology of at least approximately 80%, and in particular 85%, with the region comprised between the amino acids in positions (33) and (338) of the sequence SEQ ID NO: 2, providing that this homologous sequence exhibits an angiogenesis-inhibiting activity.

15. (new) A pharmaceutical composition characterized in that it contains as active ingredient:

- a protein characterized in that it comprises or is constituted by:

- * a fragment of the NOV protein, represented by the sequence SEQ ID NO: 2, providing that this fragment exhibits an angiogenesis-inhibiting activity, said fragment comprising in particular approximately 40 to approximately 180 amino acids, and being in particular represented by one of the following sequences SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10 or SEQ ID NO: 12, or

- * any sequence derived from the sequence SEQ ID NO: 2 or from a fragment defined below, in particular by substitution, deletion or addition of one or more amino acids, providing that this derived sequence exhibits an angiogenesis-inhibiting activity, or

- * any sequence homologous to the sequence SEQ ID NO: 2 or to a fragment defined below, preferably having a homology of at least

approximately 80%, and in particular 85%, with the region comprised between the amino acids in positions (33) and (338) of the sequence SEQ ID NO: 2, providing that this homologous sequence exhibits an angiogenesis-inhibiting activity, or

– a nucleotide sequence characterized in that it comprises or is constituted by a nucleotide sequence coding:

- * either for the NOV protein as defined above,
- * or for a fragment of the NOV protein as defined above,
- * or for a sequence derived from the NOV protein as defined above,
- * or for a sequence homologous to the NOV protein as defined above,

said nucleotide sequence corresponding in particular to the nucleotide sequence SEQ ID NO: 1 coding for SEQ ID NO: 2, or to the sequence SEQ ID NO: 3 coding for SEQ ID NO: 4, or to the sequence SEQ ID NO: 5 coding for SEQ ID NO: 6, or to the sequence SEQ ID NO: 7 coding for SEQ ID NO: 8, or to the sequence SEQ ID NO: 9 coding for SEQ ID NO: 10, or to the sequence SEQ ID NO: 11 coding for SEQ ID NO: 12, or

– an anti-idiotypic antibody of the NOV protein,
in combination with a pharmaceutically acceptable vector.

16. (new) The pharmaceutical composition according to claim 15, characterized in that it contains as active ingredient a protein characterized in that it comprises or is constituted by:

* a fragment of the NOV protein, represented by the sequence SEQ ID NO: 2, providing that this fragment exhibits an angiogenesis-inhibiting activity, said fragment comprising in particular approximately 40 to approximately 180 amino acids, and being in particular represented by one of the following sequences SEQ ID NO: 4, SEQ ID NO: 6,

SEQ ID NO: 8, SEQ ID NO: 10 or SEQ ID NO: 12, or

* any sequence derived from the sequence SEQ ID NO: 2 or from a fragment defined above, in particular by substitution, deletion or addition of one or more amino acids, providing that this derived sequence exhibits an angiogenesis-inhibiting activity, or

* any sequence homologous to the sequence SEQ ID NO: 2 or to a fragment defined above, preferably having a homology of at least approximately 80%, and in particular 85%, with the region comprised between the amino acids in positions (33) and (338) of the sequence SEQ ID NO: 2, providing that this homologous sequence exhibits an angiogenesis-inhibiting activity,

in combination with a pharmaceutically acceptable vector.

17. (new) The pharmaceutical composition according to claim 15, characterized in that it contains as active ingredient the sequence SEQ ID NO: 8.

18. (new) A method for the treatment:

- of pathologies requiring the inhibition of endothelial proliferation, in particular within the framework of the following pathologies: age-related macular degeneration, diabetic retinopathy, rheumatoid arthritis, angiomas, angiosarcomas, in particular Castelman's disease and Kaposi's sarcoma, or

- of pathologies requiring the inhibition of endothelial activation, in particular within the framework of the following pathologies: allograft and xenograft rejection, acrocyanosis, scleroderma, or within the framework of the preparation of grafts between collection and transplantation,

said method comprising the administration of a pharmaceutical composition characterized in that it contains as active ingredient:

- a protein characterized in that it comprises or is constituted by:

- * a fragment of the NOV protein, represented by the sequence SEQ ID NO: 2, providing that this fragment exhibits an angiogenesis-inhibiting activity, said fragment comprising in particular approximately 40 to approximately 180 amino acids, and being in particular represented by one of the following sequences SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10 or SEQ ID NO: 12, or

- * any sequence derived from the sequence SEQ ID NO: 2 or from a fragment defined below, in particular by substitution, deletion or addition of one or more amino acids, providing that this derived sequence exhibits an angiogenesis-inhibiting activity, or

- * any sequence homologous to the sequence SEQ ID NO: 2 or to a fragment defined below, preferably having a homology of at least approximately 80%, and in particular 85%, with the region comprised between the amino acids in positions (33) and (338) of the sequence SEQ ID NO: 2, providing that this homologous sequence exhibits an angiogenesis-inhibiting activity, or
 - a nucleotide sequence characterized in that it comprises or is constituted by a nucleotide sequence coding:
 - * either for the NOV protein as defined above,
 - * or for a fragment of the NOV protein as defined above,
 - * or for a sequence derived from the NOV protein as defined above,
 - * or for a sequence homologous to the NOV protein as defined above,said nucleotide sequence corresponding in particular to the nucleotide sequence SEQ ID NO: 1 coding for SEQ ID NO: 2, or to the sequence SEQ ID NO: 3 coding for SEQ ID NO: 4, or to the sequence SEQ ID NO: 5 coding for SEQ ID NO: 6, or to the sequence SEQ ID NO: 7 coding for SEQ ID NO: 8, or to the sequence SEQ ID NO: 9 coding for SEQ ID NO: 10, or to the sequence SEQ ID NO: 11 coding for SEQ ID NO: 12, or
 - an anti-idiotypic antibody of the NOV protein,
- in combination with a pharmaceutically acceptable vector,
- said pharmaceutical composition being administered at a rate of approximately 0.1 to approximately 20 mg/kg/day.